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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/523,776	03/11/2000	Pamela L. Zeitlin	49632 71699	5882

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EDWARDS ANGELL PALMER & DODGE LLP
P.O. BOX 55874
BOSTON, MA 02205

EXAMINER	
WANG, SHENGJUN	
ART UNIT	PAPER NUMBER
1617	
MAIL DATE	DELIVERY MODE
12/27/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/523,776	ZEITLIN ET AL.	
	Examiner	Art Unit	
	Shengjun Wang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 September 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *48,51 and 55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *48,51,55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt of applicants' remarks and exhibits submitted September 28, 2007 is acknowledged.

Claim Rejections 35 U.S.C. 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 48, 51 and 55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Herron (US Patent 4,764,521) in view of Rubenstein et al (IDS, CJ) and Rephaeli (U.S. Patent 5,939,455).

3. Herron teaches generally that substituted aryl carboxylic acids, including substituted 4-phenyl-3-butenoic acid are known to be useful for treating respiratory disease such as cystic fibrosis. See, the abstract, columns 1-4, column 12, lines 5, column 17, lines 50-52.

4. Herron does not teach expressly the employment of unsubstituted aryl carboxylic acid, e.g., 4-phenyl-trans-3-butenoic acid for treatment of cystic fibrosis.

5. However, Rubbenstein et al. teaches unsubstituted aryl carboxylic acid, 4-phenylbutyric acid is also known to be useful for treatment of cystic fibrosis. See, particularly, the abstract. Rephaeli further teaches that a variety of butyric acid derivatives, including phenyl-butyric acid, cinnamic acid, isobutyramide, phenylacetic acid, vinyl acetic acid, etc, are known to be useful for treatment of cystic fibrosis. See, particularly, column 1, lines 15-29, column 10, lines 17-23, and the claims.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to employ 4-phenyl-trans-3-butenoic acid for treating cystic fibrosis.

A person of ordinary skill in the art would have been motivated to employ 4-phenyl-trans-3-butenoic acid for treating cystic fibrosis because aryl carboxylic acids, with substituent or without substituent on the aryl ring, and wherein the carboxyl group attached to the aryl group through either alkyl or alkenyl, are generally known to be useful for treating cystic fibrosis. The instant compound differing from the prior art compound only in the substituent on the aryl ring, or the double bond at the linker between the aryl and carboxylic group, would have been reasonably expected to be similarly useful for treating cystic fibrosis, absent evidence to the contrary. Regarding claim 22-23, note selecting and/or optimizing an administering method of a pharmaceutical agent is considered within the skill of artisan.

6. Claims 48, 51 and 55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Faller et al. (WO 99/40883).

7. Faller teaches a method of treating cystic fibrosis comprising administering to a composition comprising butyric acid derivatives, e.g., cinnamic acid. See, particularly, the abstract and the claims.

8. Faller does not teach expressly to employ the particular compounds herein, e.g., 4-phenyl-3-butenoic acid.

9. The reference teaches certain compounds that are structural homologs of the instantly claimed compounds, i.e., they differ only by a CH_2 group. Cinnamic acid differs from 4-phenyl-3-butenoic acid by a methylene moiety. The instant compounds are structural homologs of the

reference compounds. One having ordinary skill in the art would have been motivated to prepare the instantly claimed compound because such structurally homologous compounds are expected to possess similar properties. It has been held that compounds that are structurally homologous to prior art compounds are prima facie obvious, absent a showing of unexpected results. In re Hass, 60 USPQ 544 (CCPA 1944); In re Henze, 85 USPQ 261 (CCPA 1950). Note both 4-phenyl-2-butenic acid or 4-phenyl-3-butenic acid are homologs to cinnamic acid. It should be well understood that cinnamic acid present either in trans or cis form. Therefore, without a particular limitation, cinnamic acid would encompass both trans and cis forms.

Response to the Arguments

Applicants' remarks and exhibit (Zetilin's review article) submitted September 28, 2007 have been fully considered, but are found unpersuasive as to the establishment of a prima facie case of unexpected benefit residing in the claimed invention, sufficient to rebut the rejections on the record.

As stated in the prior office action, For the establishment of unexpected results, a few notable principles are well settled. It is applicant's burden to explain any proffered data and establish how any results therein should be taken to be unexpected and significant. See MPEP 716.02 (b). Particularly, the claimed invention is directed to a method of treating cystic fibrosis by administering to the patient a therapeutically effective amount of trans-SAA. Applicants cite Zeitlin article as evidence that F508 mutation results in misprocessing of CFTR chloride channel in the endoplasmic reticulum and subsequent degradation of the protein, and absence of CFTR on the cell membrane is associated with chloride and sodium imbalance. However, even with these facts, the evidences presented in the declaration are still not sufficient to the establishment

of a prima facie case of unexpected benefit residing in the claimed invention, sufficient to rebut the rejections on the record. The applicant produced single pointed data in the declaration shows that trans-SAA has superior property as to promoting the trafficking of F508-CFTR to the cell surface relative to cinnamic acid and 4-PBA. It is particularly noticed that cinnamic acid is inferior to the control. However, the cited references teaches that cinnamic acid is useful for treatment of cystic fibrosis. There is no evidence on the record shows that the mechanism disclosed by Zeitlin is the only biological pathway for treatment of cystic fibrosis. Applicant provide no explanation as to why cinnamic acid, a compound known to be useful for treatment of cystic fibrosis, is negative in this in vitro method. Further, even assumed applicant had establish that the biological pathway cited by Zeiltin is the solo pathway for treatment of cystic fibrosis, it is well settled patent law "that it is not a difficult matter to carry out a process in such a fashion that it will not be successful and, therefore, the failures of experimenters who have no interest in succeeding should not be accorded great weight" In re Michalek, 74 USPQ 108, at 109 citing Bullard Company et al v. Coe, 147 F.2d. 568, 64 USPQ 359." (see also MPEP 716.07) Therefore, applicant's showing of inactivity of cinnamic acid lack a probative force for establishing an unexpected result.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shengjun Wang whose telephone number is (571) 272-0632. The examiner can normally be reached on Monday to Friday from 7:00 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Shengjun Wang
Primary Examiner
Art Unit 1617

S. Wang

SHENGJUN WANG
PRIMARY EXAMINER